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A 76 year old male with an unusual presentation of merkel cell carcinoma

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ABSTRACT

INTRODUCTION: Merkel Cell Carcinoma is an aggressively malignant, neuroendocrine-derived, cutaneous neoplasm that commonly affects sun-exposed areas of the elderly population. MCC typically presents as a rapidly enlarging, painless nodule that is red to purple in color and located on sun exposed areas such as the head, neck and arms. Although rare, cases of MCC on non-sun exposed skin have been documented and typically have a worse prognosis.

PRESENTATION OF CASE: We report an atypical case of Merkel Cell Carcinoma originating in a non-sun exposed area of the body with evidence of distant metastasis. A 76-year-old male presented with complaints of a firm lesion in his left gluteal fold.

DISCUSSION: Clinical diagnosis of MCC is usually made from a combination of history and physical, skin and nodal examination, biopsy sample with H&E prep, and immunopanel. Treatment according to the National Comprehensive Cancer Network® (NCCN®) is directed by lymph node involvement and metastasis.

CONCLUSION: With initial unsuccessful treatment, his lesion was excised and pathological evaluation reported Merkel Cell Carcinoma (MCC). Despite further surgical excision and adjuvant chemotherapy, increased hyper metabolism was found in the left descending colon and left prostate of unknown etiology. There have been reports of metastasis of primary MCC to the small bowel mesentery; therefore new focal hyper metabolism cannot be delineated precisely as unrelated to MCC until biopsy and histochemical staining are performed.

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1. Introduction

Merkel Cell Carcinoma (MCC) is an aggressively malignant, neuroendocrine-derived, cutaneous neoplasm that commonly affects sun-exposed areas of the elderly population [1]. The etiology is likely multifactorial with immunosuppression, UV-induced skin damage, and viral factors, such as Merkel Cell Polyomavirus (MCPyV) contributing to the development of this neoplasm [1,2]. Occurrence of MCC is rare, but it does have the fastest increasing incidence of all skin cancers showing a 0.15–0.44 per 100,000 increase from 1986 to 2001 [3]. MCC typically presents as a rapidly enlarging, painless nodule that is red to purple in color and located on sun exposed areas such as the head, neck and arms [4]. Although rare, cases of MCC on non-sun exposed skin have been documented and typically have a worse prognosis [5]. The risk for developing MCC is increased in the elderly and male populations, as well as in

those with high UV exposure or who are immunosuppressed [4]. This malignancy almost exclusively affects Caucasian populations, with 98% of all cases occurring in this demographic, suggesting possible protection by darker skin pigmentation [6]. Early locoregional metastasis is typical of MCC and is associated with 5 year survival rate of 50% [7]. Once MCC has undergone distant metastasis the 1 year survival rate drops to 44% [7].

2. Presentation of case

2.1. Initial presentation

A 76 year old, Caucasian male presented to his primary care physician one-month post-op from an orthopedic back procedure with a chief complaint of a sore in the inner crease of his left gluteus. The patient stated that the sore had remained the same size over the previous month, and it was noted on physical exam to be a firm, red nodule that was not warm to the touch. The lesion was also moveable and elicited a stinging sensation on palpation. An initial diagnosis of cellulitis with abscess was made and the patient was started on a ten-day course of TMP-Sulfamethoxazole.

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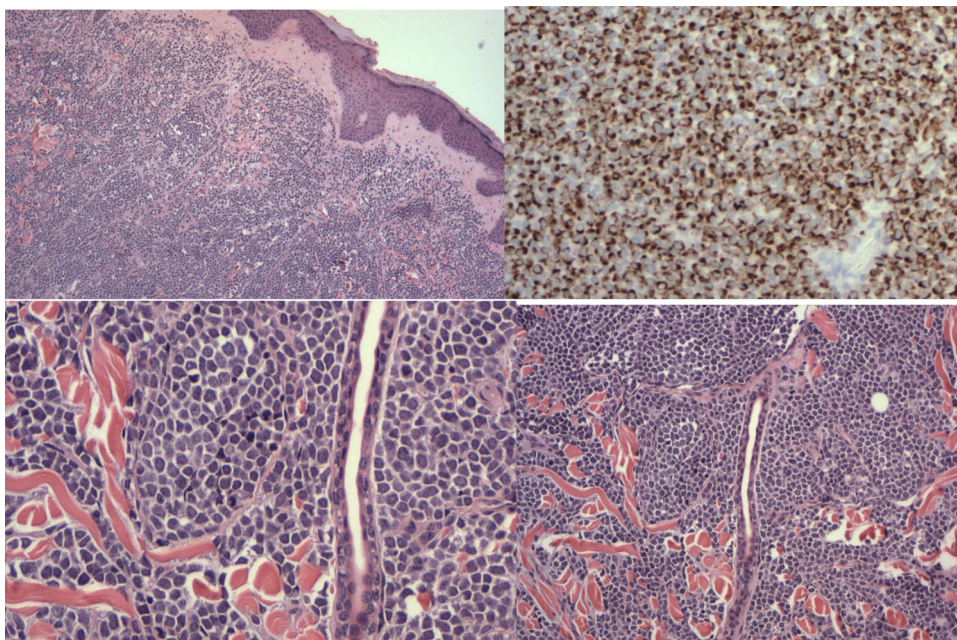


Fig. 1. Excisional biopsy of the lesion located in the left gluteal crease revealed Merkel Cell Carcinoma with positive margins (02/11/2015).

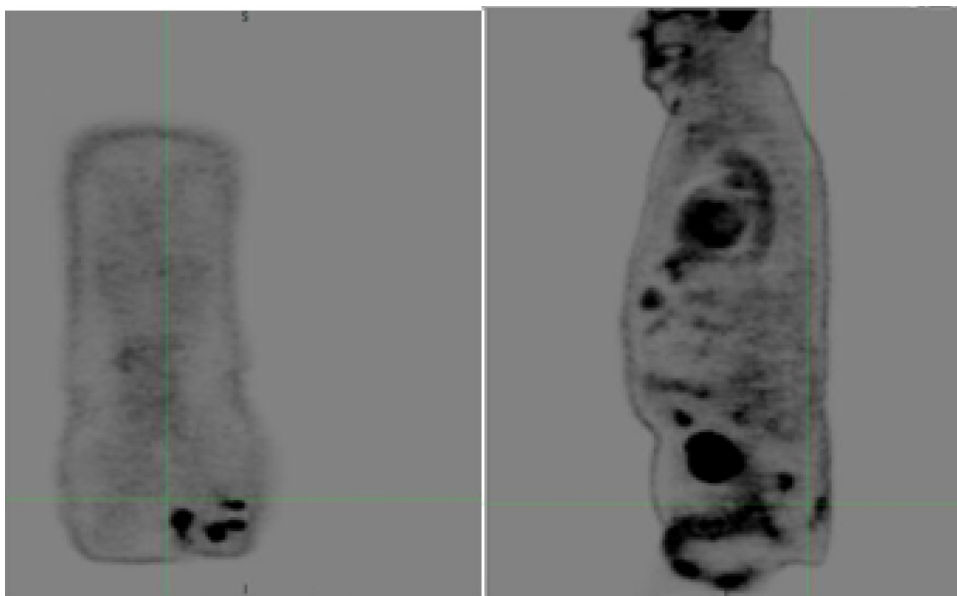


Fig. 2. Images of the PET scan one month post-surgical excision showing largest masses measuring 2.3×1.8 cm and 2×2 cm with SUV max values of 13.3 and 10.4 respectively (4.13.15).

At a follow-up appointment one week later it was revealed that the lesion no longer stung, but that the patient was still distressed by its presence. The patient was then referred to a plastic surgeon with a suspected diagnosis of cellulitis and abscess with associated fat necrosis. Surgical excision of the lesion was completed one month after the patient's initial visit. Pathological evaluation of the specimen following excision revealed a diagnosis of Merkel cell carcinoma with positive margins (Fig. 1).

2.2. Treatment course

A second surgical procedure took place two weeks later in order to obtain negative margins confirmed by frozen section. A PET scan performed one month later revealed several subcutaneous masses

involving the left buttock extending to the midline (Fig. 2). Additionally, a 2.1 cm left external iliac inguinal node showed a SUV max of 15.7. Three weeks following the PET scan, the patient underwent a radical resection of his bilateral buttocks in addition to a sentinel node procedure. Negative margins were achieved and two positive nodes were removed. A second PET scan performed two months later revealed a nodule in the right lung in addition to a nodular focus in the subcutaneous adipose tissue of the left gluteal region (Fig. 3). This scan also showed a right inguinal node.

2.3. Adjuvant therapy

Two weeks later the patient began a two-month course of chemotherapy consisting of Cisplatin and Etoposide. Two weeks

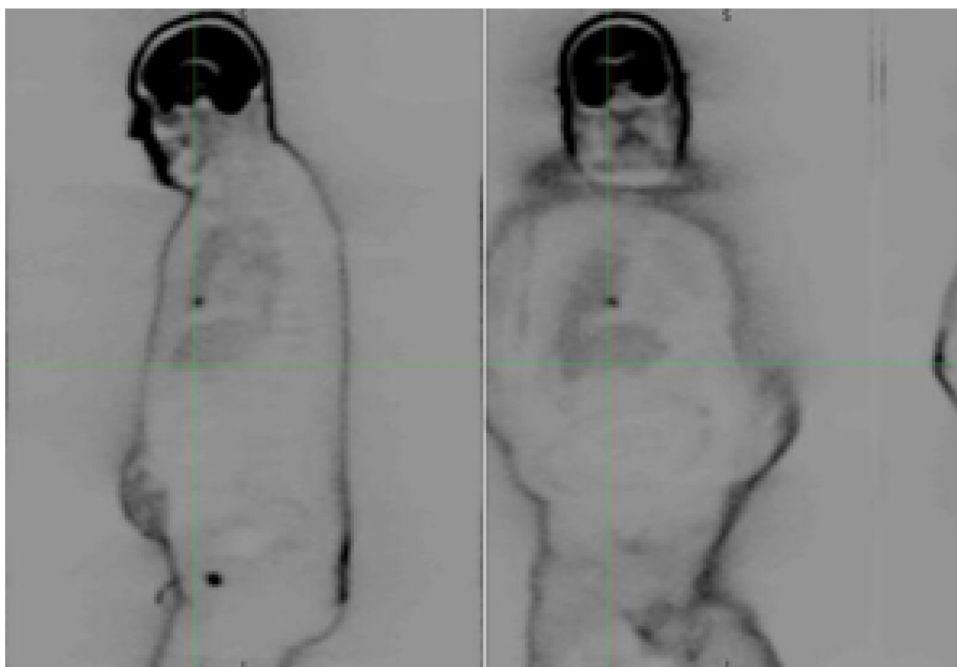


Fig. 3. A second PET scan performed after the third radical resection revealing a 1.7×0.6 cm nodule with a SUV max of 3.12 in the right lung in addition to a 9 mm nodular focus in the subcutaneous adipose tissue of the left gluteal region with a SUV max of 3.5. A right inguinal node was also present measuring 2.6×1.8 cm with a SUV max of 13.29 (7.08.15).

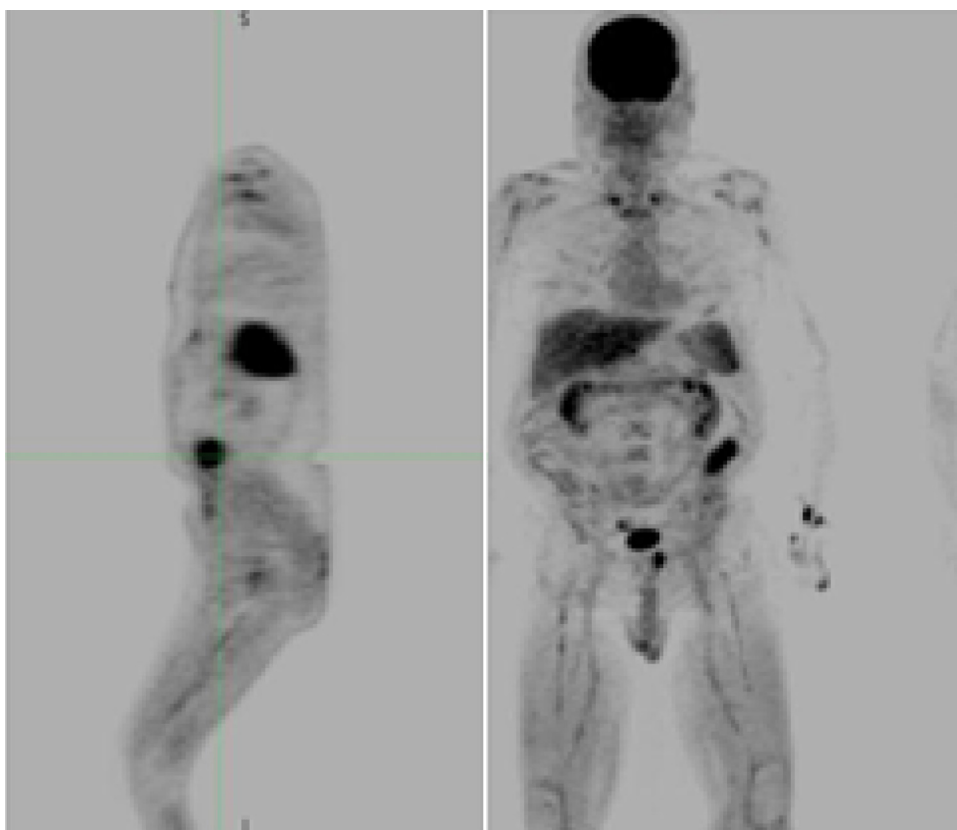


Fig. 4. Third PET scan showing resolution of the right middle lobe lung nodule as well as interval resolution of the right inguinal node measuring 1.7×0.8 cm with a SUV max of 1.59. The left gluteal hyperdensity in the subcutaneous adipose tissue measured an SUV max of 2.0, but this is decreased from its SUV max value of 5.27 on a previous scan. Increased metabolism is noted in the descending colon and left lateral prostate (10.05.15).

following completion of the patient's chemotherapy, a third PET scan was performed. The scan revealed interval resolution of both the previously identified lung nodule as well as the right inguinal

node. The left gluteal region showed some hyper density in the subcutaneous adipose tissue, but shows a reduction in comparison to the previous scan. The scan also revealed increase splenic uptake,

which was thought to be the result of chemotherapy. Incidental findings of focal hyper metabolism in the descending colon and left lateral aspect of the prostate were also noted (Fig. 4).

3. Discussion

3.1. Diagnosis

Clinical diagnosis of MCC is usually made from a combination of history and physical, skin and nodal examination, biopsy sample with H&E prep, and immunopanel [8]. Due to the non-specific, benign clinical appearance of the initial lesion, MCC is seldom suspected prior to biopsy [9]. An appropriate immunopanel should include CK20 and thyroid transcription factor-1 (TTF-1) [8]. Immunohistochemistry for CK20 and most low-molecular-weight cytokeratin markers (pancytokeratins AE1/AE3) are typically positive [8].

After diagnosis of MCC, clinical workup involves imaging studies to identify and quantify regional and distant metastasis. PET-CT is the preferred imaging technique according to some studies. If PET-CT is unavailable, CT or MRI may be used [8].

3.2. Treatment

Treatment according to the National Comprehensive Cancer Network® (NCCN®) is directed by lymph node involvement and metastasis [8]:

Clinical N0 – Management of the primary tumor is wide local excision with adjuvant radiation therapy to the primary tumor site. Sentinel lymph node biopsy evaluation with immunopanel is performed for management of the draining nodal basin.

Clinical N+ – Fine needle aspiration (FNA) or core biopsy is performed with immunopanel. Imaging studies or open biopsy are considered when the FNA is positive or negative respectively. Node dissection and radiation therapy is performed for positive nodal involvement without distant metastasis. Follow up visits should include complete skin and lymph node exam every 3–6 months for 2 years, then every 6–12 months thereafter for recurrence.

Clinical M1 – A combination of excision, regional radiation therapy and chemotherapy is considered. Cisplatin and Etoposide are used in combination. Clinical trials are preferred if available.

3.3. Clinical trials

Numerous trials are underway in search of advancement in therapy. Pembrolizumab, a programmed death receptor antagonist used to combat other forms of cancer, is currently undergoing a clinical trials [10]. The death receptor is a molecule expressed by lymphocytes that when bound by its ligand can suppress the immune system's ability to combat cancer [11]. By blocking the receptor-ligand interaction, Pembrolizumab is aimed at decreasing immune-suppression and thus increasing the body's ability to fend off neoplastic cells. Additionally there are trials using Cabozantinib, which is a MET/VEGFR2 inhibitor [12]. MET/VEGFR2 are molecules involved in angiogenesis and cell survival/motility, which all play a key role in the progression of neoplasia [12]. Finally, it has been hypothesized that infusion of autologous CD8-positive T cells that are primed for MCPyV Ag along with concurrent IL-2 therapy may be a new mechanism to target therapy against Merkel cell carcinoma [13]. The Merkel cell polyomavirus (MCPyV) is theorized to integrating in to the host cell's genome leading to clonal expansion, all the while preventing viral replication via a mutation to ensure host cell survival [14,15].

4. Conclusion

This patient presented with a unique case of Merkel cell carcinoma. Although he is elderly, the location of the lesion and the fact that he is immunocompetent with no comorbid illness, suggests an atypical presentation of MCC. It is not clear whether his incidental findings of focal hyper metabolism in the descending colon and left prostate are related to MCC at this time. There have been reports of metastasis of primary MCC to the small bowel mesentery, therefore new focal hyper metabolism cannot be delineated precisely as unrelated to MCC until biopsy and histochemical staining are performed [9].

Surgical debridement was performed initially, but adjuvant radiotherapy was delayed due to the initial uncertainty of the diagnosis. Due to systemic metastasis of MCC, chemotherapy was initiated prior to radiation therapy once the diagnosis was made. After 2 months in remission this cancer relapsed, consistent with its aggressively malignant nature. We will continue to follow pending further investigation of the descending colon. It is our hope that with increased knowledge and awareness of atypical presentations of Merkel cell carcinoma, we can detect and address this disease in its infancy prior to any metastasis and spare future patients the same clinical course.

Update: Since relapse, the patient's condition deteriorated. 14 months since diagnosis, the patient has passed away from complications of Merkel Cell Carcinoma.

Conflicts of interest

The authors have no conflicts of interest.

Funding

None.

Ethical approval

No research study performed on patient.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Joel Acab and Dr. Chukwuma Ebo were involved in the patient care.

Joel Acab and Wade Kvatum researched and wrote the article. All authors reviewed and approved the final manuscript.

Guarantor

Dr. Chukwuma Ebo, MD.

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